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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,430	09/19/2006	Yoon Jeong Park	4240-149	7380

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER	
KEMMERER, ELIZABETH	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,430	PARK ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,10-13,19,21 and 22* is/are pending in the application.

4a) Of the above claim(s) *2,3,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,13,19,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment of 03 August 2009 has been entered in full. Claims 1, 4-9, 14-18, and 20 are canceled. Claims 2, 3, 11, and 12 remain withdrawn from consideration as being directed to a non-elected species. Applicant's comments regarding the status of the withdrawn claims are noted. Applicant is advised that, if a generic claim is found allowable, withdrawn claims that depend therefrom or otherwise include all the limitations of the allowable generic claim will be rejoined accordingly. See MPEP § 809.02(a), MPEP § 811.04, 37 CFR 1.141, and 37 CFR 1.142(b).

Claims 10, 13, 19, 21, and 22 are under examination.

Withdrawn Objections And/Or Rejections

The objections to claims 1, 5, 10, and 14 for informalities as set forth at p. 4 of the previous Office action (mailed 03 February 2009) is *withdrawn* in view of the amended and canceled claims (received with the response of 03 August 2009).

The rejection of claims 4 and 13 under 35 U.S.C. § 112, second paragraph, for indefiniteness as set forth at p. 4 of the previous Office action (mailed 03 February 2009) is *withdrawn* in view of the amended and canceled claims (received with the response of 03 August 2009).

The rejection of claims 1, 4, 7, 10, 13, 16, 17, and 18 under 35 U.S.C. § 103(a) as being unpatentable over US 6,409,764 B1 in view of WO 2005/113585 A2 as set forth at pp. 6-7 of the previous Office action (mailed 03 February 2009) is *withdrawn* in

view of the amended and canceled claims (received with the response of 03 August 2009).

Specification

The specification remains objected to because of the following informalities: the text of the specification discusses various fragments of BMP proteins and then refers to a sequence identifier. However, there is a lack of correspondence between the discussion of fragments and proteins and the sequences appearing in the sequence listing.

Applicant's response has helpfully resolved the inconsistencies regarding elected SEQ ID NO: 6 as well as several other fragments. However, the paragraph submitted as a replacement to the paragraph of the specification at p. 4, line 21 to p. 5, line 10 contains several typographical errors that should be corrected. Specifically:

- 3rd line: "SEQ ID NO: 61;" should be "SEQ ID NO: 6]"

- 6th line: "SEQ ID NO: lo" should be "SEQ ID NO: 10"

- 9th line: "293-3 13" should be "293-313" (remove extra space)

-11th line: "9 1- 11 0" should be "91-110" (remove extra spaces)

- 12th line: "397-41 8" should be "397-418" (remove extra space)

- 14th line: "98-1 17" should be "98-117" (remove extra space)

Furthermore, the direction to enter a replacement paragraph at p. 4, lines 24-26 was improper because the replacement paragraph is completely different from the text

at p. 4. It appears that the replacement paragraph was intended to replace text at p. **5**, lines 24-26.

Appropriate correction is required. New matter must be avoided.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 (and dependent claims 13, 19, 21, and 22) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 10 has been amended to recite a CGC spacer. The specification as originally filed does not provide adequate written description of this spacer. There may be a typographical error in claim 10, wherein "CGC" was intended to be "CGG." Amending the claim to recite "CGG" would be remedial.

Priority

Applicant's claim for priority to Korean document 10-2004-0019010, filed 19 March 2004 is noted. The certified copy of this document was received on 19

September 2006 and the certified partial translation was received with the response of 03 August 2009.

Upon consideration of the partial translation, it is determined that the Korean document does not provide adequate written description or enablement for elected SEQ ID NO: 6.

Therefore, priority is denied to Korean document 10-2004-0019010, filed 19 March 2003. The effective filing date of the instant application is determined to be that of the PCT/KR05/00801 document, 18 March 2005.

35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 10, 13, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over **US 6,409,764 B1** (White et al.; issued 25 June 2002) in view of **WO 2005/113585 A2** (Acceleron Pharma Inc., or "Knopf"; published in English 11 December 2005; international filing date 20 May 2005 designating the US; earlier effective US filing date 20 May 2004), **Gauvreau et al.** (2004, Bioconjugate Chem. 15:1146-1156) and **US 6,316,003 B1** (Frankel et al.; issued 13 November 2001).

'764 teaches a bone graft material or scaffold for tissue engineering applications such as implants comprising BMP-2 immobilized on the surface. The material is a biocompatible polymer that is porous. See col. 24-27, Example 2. See especially col. 25, lines 24-49, treatment (iii). '764 also teaches membranes made of polylactic acid. See col. 14, lines 46-54. '764 does not teach immobilizing a particular concentration of peptide, a fragment of BMP-2 (namely, elected SEQ ID NO: 6), a CGG spacer at the N-terminus, or modifying the implant surface by oxidation and nitrification to facilitate adhesion of the peptide to the surface.

However, '585 teaches the exact BMP-2 fragment of SEQ ID NO: 6 at p. 20, line 4. Gauvreau et al. discusses the use of sulfo-SMCC to achieve cross-linking of a cysteine-containing protein to a solid substrate in order to immobilize the protein. Gauvreau et al. also teach oxidation and nitrification to facilitate adhesion of proteins to solid supports. '003 teaches the addition of CGG to the N-terminus of a tat protein fragment that lacked a cysteine, and the use of sulfo-SMCC modified ribonuclease to achieve a cross-linking reaction. See col. 32, lines 36-61.

Regarding the recited concentration range of 0.1-10 mg/cm^2, optimization of ranges is considered well within the ordinary level of skill in the art, and is thus obvious absent evidence of unexpected results. See M.P.E.P. § 2144.05, section II, OPTIMIZATION OF RANGES.

Therefore, given that the level of skill in the medical arts is very high and in the absence of unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the material of '764 by using the BMP-2 fragment disclosed by '585 and the CGG-linker/sulfo-SMCC system for cross-linking as suggested by Gauvreau et al. and '003 with a reasonable expectation of success. This is because known work in one field of endeavor was known to prompt variations of it for use in the same field to achieve predictable results. As noted by the United States Supreme Court, if a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. *KSR,* 127 S. Ct. at 1740. "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known

options within his or her technical grasp. If this leads to the anticipated success, it is likely the product is not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show it was obvious under 35 U.S.C. 103." *KSR Int'l Co. v. Teleflex Inc.,* 127 S.Ct. 1727, 1742, 82USPQ2d 1385, 1396 (2007).

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over **US 6,409,764 B1** (White et al.; issued 25 June 2002) in view of **WO 2005/113585 A2** (Acceleron Pharma Inc., or "Knopf"; published in English 11 December 2005; international filing date 20 May 2005 designating the US; earlier effective US filing date 20 May 2004), **Gauvreau et al.** (2004, Bioconjugate Chem. 15:1146-1156) and **US 6,316,003 B1** (Frankel et al.; issued 13 November 2001) as applied to claims 10, 13, 21, and 22 above, and further in view of **Puleo et al.** (2002, Biomaterials 23:2079-2087).

As discussed above, '764 teaches a bone graft material or scaffold for tissue engineering applications comprising BMP-2 immobilized on the surface, '585 teaches the elected BMP-2 fragment, SEQ ID NO: 6, Gauvreau et al. teach immobilization by sulfo-SMCC, and '003 teaches the addition of CGG to the N-terminus.

'764 does not teach the use of titanium implant materials. However, such was known in the prior art. For example, Puleo et al. teaches a titanium implant on which was cross-linked BMP-4 for the purpose of developing orthopedic and dental implants that induced bone formation.

Therefore, given that the level of skill in the medical arts is very high and in the absence of unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the material of '764 by using the BMP-2 fragment disclosed by '585, the immobilization technique of Gauvreau et al., and the CGG spacer of '003, by using the titanium implant material as suggested by Puleo et al. with a reasonable expectation of success. This is because known work in one field of endeavor was known to prompt variations of it for use in the same field to achieve predictable results.

Applicant's arguments (pp. 11-15, remarks received 03 August 2009) have been fully considered but are not found to be persuasive for the following reasons.

Applicant argues that the combination of White and Knopf results in a material wherein there is an undesirable burst release of growth factors. Applicant urges that the claimed invention achieves stable and lasting pharmacological effects. This is not found to be persuasive in view of the new rejections necessitated by amendment. Gauvreau et al. discusses the use of sulfo-SMCC to achieve cross-linking of a cysteine-containing protein to a solid substrate in order to immobilize the protein. Gauvreau et al. also teach oxidation and nitrification to facilitate adhesion of proteins to solid supports. '003 teaches the addition of CGG to the N-terminus of a tat protein fragment that lacked a cysteine, and the use of sulfo-SMCC modified ribonuclease to achieve a cross-linking reaction. See col. 32, lines 36-61. Thus, Gauvreau et al. and '003 also solved the problem recognized by '764.

Applicant refers to Figures 6 and 8 of White et al., arguing that White et al. merely teach placing TGF-β proteins in a space within a tissue penetrable device, and not immobilized. This ahs been fully considered but is not found to be persuasive. As taught by White et al. ('764) at col. 25, third paragraph, treatment iii involved pretreatment of ePTFE and PGA:TMC membranes by coating with polyethylene imine, followed by cross-linking with ethylene glycol bis[succinimidyl-succinate] (EGS) and then adding BMP-2 with sulfo-EGS to reversibly cross-link the BMP-2. Gauvreau et al. and '003 taught a superior cross-linking method such that the undesirable burst effect would have been addressed.

Applicant argues that Gauvreau et al. and Frankel et al. ('003) fail to correct the alleged deficiencies of White and Knopf. Specifically, Applicant argues that Korean foreign priority document 10-2004-0019010 provides for oxidation and nitrification to facilitate adhesion of the active peptide to the surface of the implant material. Applicant urges that the effective filing date of the claimed invention is 19 March 2004, thus predating the Gauvreau et al. reference, which was published 20 August 2004. This has been fully considered but is not found to be persuasive. The Korean foreign priority document has been reviewed and was found to lack support for all of the features recited in the instant claims. For example, the Korean document does not disclose the elected fragment of BMP-2. Similarly, there is no support for the limitation of 0.1-10 mg/cm^2 for the concentration of the peptide on the implant surface. Therefore, priority is denied to the Korean foreign priority document, and Gauvreau et al. qualifies as prior art.

Applicant argues that the teachings of Puleo et al. fail to correct the alleged deficiencies of White and Knopf. This argument has been fully considered but is not found to be persuasive, since the rejection now also relies on Gauvreau et al. and '003.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number

is (571) 272-0874. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ECK/
09 October 2009

/Elizabeth C. Kemmerer/
Elizabeth C. Kemmerer, Ph.D.
Primary Examiner, Art Unit 1646